Paper No. 18

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte BRETT P. MONIA, LEX M. COWSERT, and MUTHIAH MANOHARAN

Appeal No. 2003-0554
Application No. 09/575,554

ON BRIEF

Before ADAMS, GRIMES, and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 7-20, which are all the claims pending in the application.

Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. An oligonucleotide 8 to 30 nucleotides in length which is targeted to a nucleic acid encoding human Ki-ras, wherein said oligonucleotide is capable of inhibiting Ki-ras expression, and wherein said oligonucleotide comprides at least an 8-nucleobase portion of SEQ ID NO: 20, 21, 22, 26, 28, 31, 32 or 33.

The references relied upon by the examiner are:

Bos et al. (Bos) 4,871,838 Oct. 3, 1989

Hall et al. (Hall), "Human N-ras: cDNA cloning and gene structure," Nucleic Acids Research, Vol. 13, No. 14, pp. 5255-5268 (1985)

Inoue et al. (Inoue), "Sequence-dependent hydrolysis of RNA using modified oligonucleotide splints and RNase H," FEBS Letters, Vol. 215, No. 2, pp. 327-330 (1987)

Agrawal et al. (Agrawal), "Site-specific excision from RNA by RNase H and mixed-phosphate-backbone oligodeoxynucleotides," Proc. Natl. Acad. Sci. USA, Vol. 87, pp. 1401-1405 (1990)

Daaka et al. (Daaka), "Target Dependence of Antisense Oligodeoxynucleotide Inhibition of c-Ha-ras p21 Expression and Focus Formation in T24-Transformed NIH3T3 Cells," Oncogene Research, Vol. 5, pp. 267-275 (1990)

Uhlmann et al. (Uhlmann), "Antisense Oligonucleotides: A New Therapeutic Principle," Chemical Reviews, Vol. 90, No. 4, pp. 543-584 (1990)

Saison-Behmoaras et al. (Saison-Behmoaras), "Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation," EMBO J., Vol. 10, No. 5, pp. 1111-1118 (1991)

GROUND OF REJECTION

Claims 1 and 7-20 stand rejected under 35 U.S.C. § 103. As evidence of obviousness the examiner relies on Bos, Daaka, Hall and Saison-Behmoaras, Uhlmann, Agrawal, Inoue and Smith[1].

We reverse.

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[1] The examiner failed to identify this reference as part of the "Prior Art of Record." See Answer, pages 3-4. We were also unable to locate a copy of this reference in the administrative file. Nevertheless, for the purposes of this opinion, we rely on the examiner's characterization of the Smith reference. See Answer, page 7. Prior to any further action, we encourage the examiner to review the administrative file to insure that it is complete.

DISCUSSION

Initially, we note that appellants' composition claims, claims 7-10, depend from, and further limit claim 1 to include, inter alia, a modified oligonucleotide backbone, or a pharmaceutically acceptable carrier. In addition, appellants' method claims, claims 10-20, all require "an effective amount of an oligonucleotide of claim 1." As set forth above, claim 1 is drawn to an oligonucleotide that is 8 to 30 nucleotides in length, which is capable of inhibiting Ki-ras expression, and comprises at least an 8 nucleotide portion of SEQ ID NO: 20, 21, 22, 26, 28, 31, 32 or 33.[2]

THE REJECTION UNDER 35 U.S.C. § 103:

According to the examiner (Answer, bridging paragraph, pages 5-6), Bos discloses antisense oligonucleotides to human H-ras and Ki-ras and to regions of the ras genes corresponding to codons 12 and 61. According to the examiner (id.), these oligonucleotides may be used in methods to detect the activated forms of ras, by either hybridizing to single-stranded genomic DNA fragments or to RNA. The examiner finds (Answer, page 6), "Hall teaches the sequence of N-ras from which the specific antisense molecules are derived as well as the importance of the mutations at codons 12 and 61...." As we understand the examiner's statement, Hall describes specific antisense molecules derived from the sequence of N-ras. In addition, the examiner finds (id.), both Daaka and Saison-Behmoaras teach oligonucleotides derived from H-ras that are capable of

[2] We agree with the examiner (Answer, page 17), "when the claims are drawn to a[n] '8 nucleobase portion', then only 8 nucleobases of the SEQ ID NO[.] must be present."

inhibiting H-ras expression. The examiner relies on Uhlmann, Inoue, Agrawal and Smith to teach modified oligonucleotide molecules. Answer, pages 6-7.

However, we recognize, as does the examiner (Answer, page 7), that none of the references relied upon by the examiner teach an oligonucleotide as set forth in appellants' claimed invention. To make up for this deficiency the examiner simply concludes (id.), "[t]he specific sequences would be derived by one of ordinary skill in the art making a variety of antisense oligonucleotides targeted at the taught regions." As we understand the examiner's conclusion, since the references teach constructing antisense oligonucleotides to codons 12 and/or 61 of N-ras, H-ras and Ki-ras, as well as to the translation initiation codon site of H-ras, a person interested in constructing an antisense oligonucleotide to human Ki-ras would necessarily arrive at appellants' claimed oligonucleotide, which would then be effective in inhibiting expression of the Ki-ras gene. In our opinion, however, the evidence relied upon by the examiner is not sufficient to lead a person of ordinary skill in the art to the examiner's conclusion.

To the contrary, Bos, which in our opinion is the closest prior art reference of record, did what the examiner has suggested -- produced oligonucleotides complementary to a DNA sequence encoding a mutant Ki-ras protein which contain a single base pair mutation in the codon encoding the amino acid at positions 12 and 61. Bos, however, failed to arrive at an oligonuclotide within the scope of appellants' claimed invention. See Bos, column 4, lines 26-48. Of interest, however, is that Bos discloses sequences that are complementary to appellants' claimed oligonucleotide. For example, as illustrated below, Bos

discloses (column 4, lines 32-33) a sequence for an oligonucleotide directed at the codon encoding amino acid 12 (Bos 12) which is complementary to at least an 8 nucleobase portion of appellants' SEQ ID NO: 26 (#26), shaded regions indicate mismatches:

Bos 12:	G	T	T	G	G	A	G	C	T	A	G	T	G	G	C	G	T	A	G	G
#26:	C	A	A	C	C	T	C	G	A	C	C	A	C	C	G	C	A	T	C	C

Bos also discloses (column 4, line 43) a sequence for an oligonucleotide directed at the codon encoding amino acid 61 (Bos 61) which is complementary to at least an 8 nucleobase portion of appellants' SEQ ID NO: 28 (#28), shaded regions indicate mismatches:

Bos 61:	A	C	A	G	C	A	G	G	T	G	A	A	G	A	G	G	A	G	T	A
#28:	T	G	T	C	G	T	C	C	A	C	T	T	C	T	C	C	T	C	A	T

The examiner, however, offers no evidence or explanation as to why the prior art of record would have led a person of ordinary skill to select an oligonucleotide complementary to the oligonucleotides disclosed by Bos to be "complementary to a DNA sequence encoding a mutant K-ras protein." Bos, column 4, lines 26-31, and lines 38-42.

For the foregoing reasons, we are compelled to reverse the rejection of claims 1 and 7-20 under 35 U.S.C. § 103 over the combination of Bos, Daaka, Hall and Saison-Behmoaras, Uhlmann, Agrawal, Inoue and Smith.

OTHER ISSUES

Prior to any further prosecution, we encourage the examiner to consider the effect, if any, that Bos et al., United States Patent No. 5,591,582 ('582[3]) may have on appellants' claimed invention. The '582 patent appears to be available prior art with an effective filing date through two continuation applications to August 4, 1987. Table III, column 19 of the '582 patent appears to teach at least two "Mutation-specific Oligomers" within the scope of appellants' claim 1, for example oligomer K-12 appears to correspond to appellants' SEQ ID NO. 26, and oligomer K-61 appears to correspond to appellants' SEQ ID NO. 28.

REVERSED

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

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[3] A copy of the '582 patent is included with our decision.

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